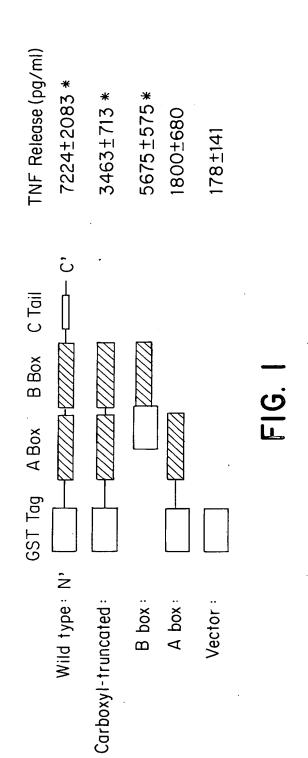
Docket/App No.: 3258.1008-001
Title: HMGB1 Combination Therapies
Inventors: Walter Newman



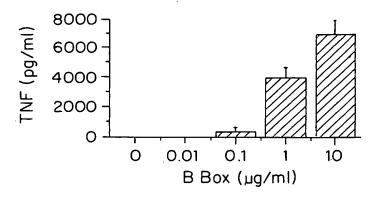


FIG. 2A

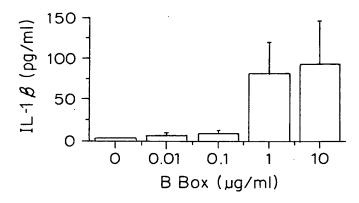


FIG. 2B

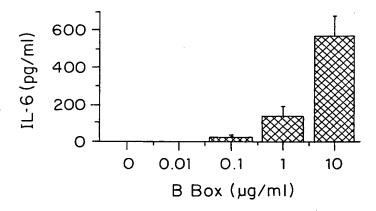
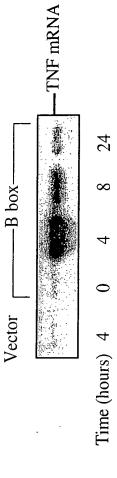


FIG. 2C

Docket/App No.: 3258.1008-001 Title: HMGB1 Combination Therapies Inventors: Walter Newman



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FIG. 2D

FIG. 2E

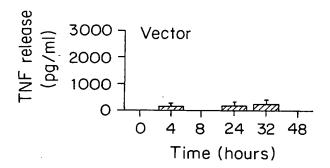


FIG. 2F

B box mutants	TNF release (pg/ml)		
B box: 74 amino acids	5675±575		
1-20	2100±756		
16-35	100±10		
30-49	120±75 100±36		
45-64			
60-74	100±20		

FIG. 3

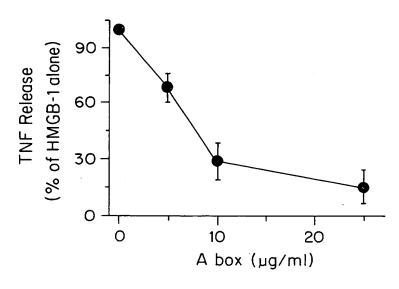


FIG. 4A

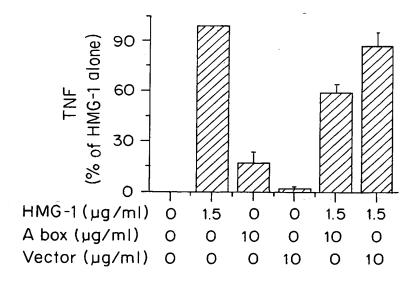


FIG. 4B

Docket/App No.: 3258.1008-001 Title: HMGB1 Combination Therapies Inventors: Walter Newman

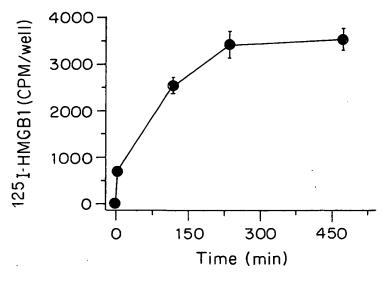


FIG. 5A

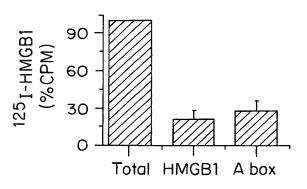


FIG. 5B

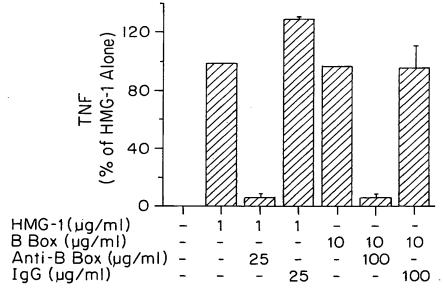


FIG. 6

Inventors: Walter Newman

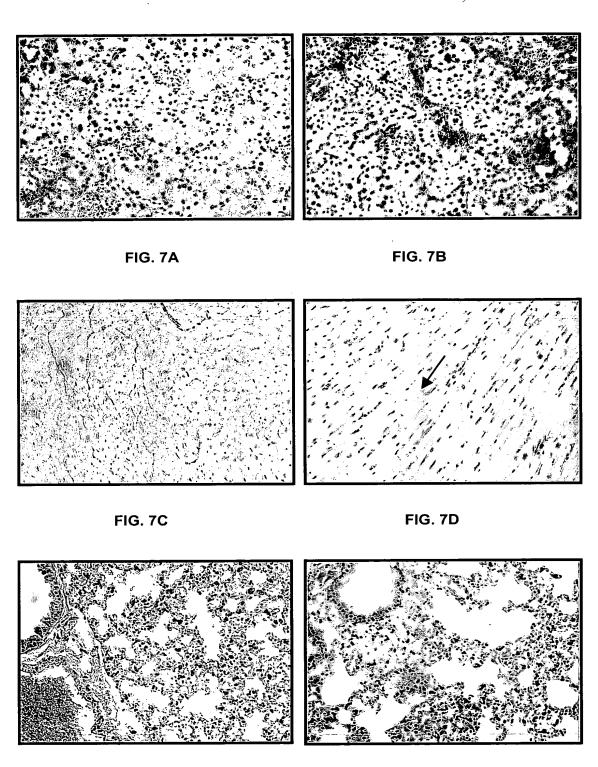


FIG. 7E FIG. 7F

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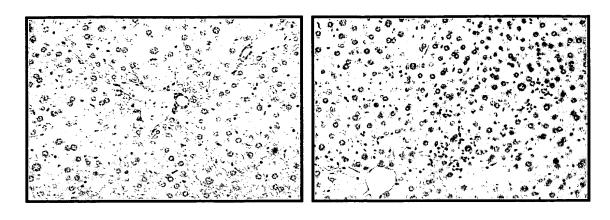


FIG. 7G FIG. 7H

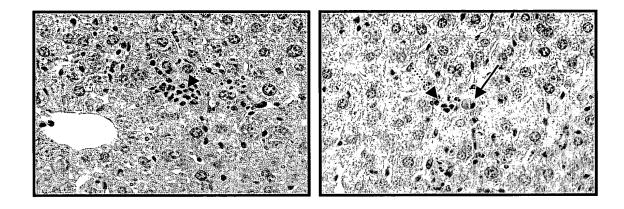


FIG. 7J

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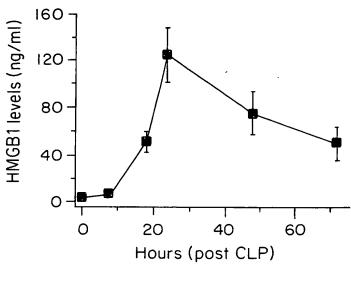


FIG. 8

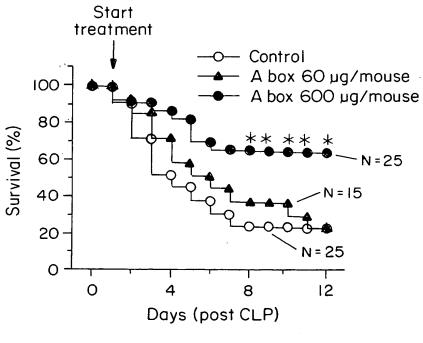


FIG. 9

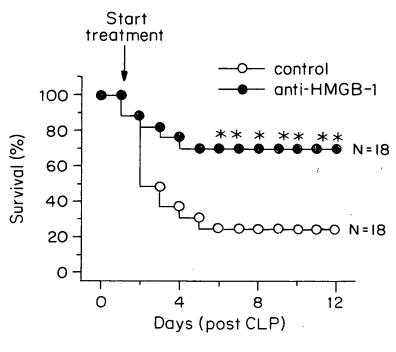


FIG. IOA

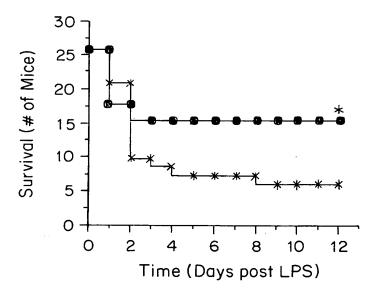


FIG. IOB

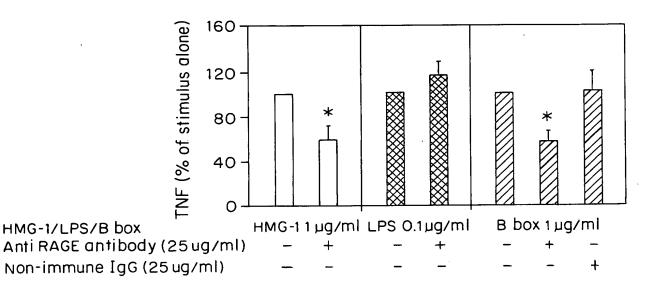


FIG. IIA

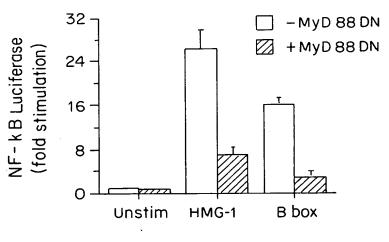


FIG. IIB

Inventors: Walter Newman

FIG. 12A

SEQ ID NO:1 - Human HMG1 amino acid sequence

1 mgkgdpkkpr gkmssyaffv qtcreehkkk hpdasvnfse fskkcserwk tmsakekgkf 61 edmakadkar yeremktyip pkgetkkkfk dpnapkrpps afflfcseyr pkikgehpgl 121 sigdvakklg emwnntaadd kqpyekkaak lkekyekdia ayrakgkpda akkgvvkaek

181 skkkkeeeed eedeedeee edeededeee dddde

FIG. 12B

SEQ ID NO:2 - Mouse and Rat HMG1 amino acid sequence

1 mgkgdpkkpr gkmssyaffv qtcreehkkk hpdasvnfse fskkcserwk tmsakekgkf 61 edmakadkar yeremktyip pkgetkkkfk dpnapkrpps afflfcseyr pkikgehpgl 121 sigdvakklg emwnntaadd kqpyekkaak lkekyekdia ayrakgkpda akkgvvkaek

181 skkkkeeedd eedeedeee eeeededeee dddde

FIG. 12C

SEQ ID NO:3 - HUMAN HMG2 amino acid sequence

1 mgkgdpnkpr gkmssyaffv qtcreehkkk hpdssvnfae fskkcserwk tmsakekskf 61 edmaksdkar ydremknyvp pkgdkkgkkk dpnapkrpps afflfcsehr pkiksehpgl 121 sigdtakklg emwseqsakd kqpyeqkaak lkekyekdia ayrakgksea gkkgpgrptg 181 skkknepede eeeeeeded eeeededee

FIG. 12D

SEQ ID NO:4 - Human, mouse and rat HMG1 A box protein sequence 1 pdasvnfsef skkcserwkt msakekgkfe dmakadkary eremktyipp kget

FIG. 12E

SEQ ID NO:5 - Human, mouse and rat HMG1 B box protein sequence 1 napkrppsaf flfcseyrpk ikgehpglsi gdvakklgem wnntaaddkq pyekkaaklk 61 ekyekdiaa

FIG. 12F

SEQ ID NO:6 - forward PCR primer for human HMG1 gatgggcaaaggagatcctaag.

FIG. 12G

SEQ ID NO:7 - reverse PCR primer for human HMG1 gcggccgcttattcatcatcatcatcttc

FIG. 12H

SEQ ID NO:8 - forward PCR primer for -C mutant of human HMG1 gatgggcaaaggagatcctaag

Docket/App No.: 3258.1008-001

Title: HMGB1 Combination Therapies

Inventors: Walter Newman

FIG. 12I

SEQ ID NO:9 - reverse PCR primer for -C mutant of human HMG1 gcggccgctcacttgcttttttcagccttgac

FIG. 12J

SEQ ID NO:10 - forward PCR primer for A+B boxes mutant of human HMG1 gagcataagaagaagcaccca

FIG. 12K

SEQ ID NO:11 - reverse PCR primer for A+B boxes mutant of human HMG1 geggeege teacttgetttttteageettgae

FIG. 12L

SEQ ID NO:12 - forward PCR primer for B box mutant of human HMG1 aagttcaaggatcccaatgcaaag

FIG. 12M

SEQ ID NO:13 - reverse PCR primer for B box mutant of human HMG1 gcggccgctcaatatgcagctatatccttttc

FIG. 12N

SEQ ID NO:14 - forward PCR primer for N'+A box mutant of human HMG1 gatgggcaaaggagatcctaag

FIG. 12O

SEQ ID NO:15 - reverse PCR primer for N'+A box mutant of human HMG1 tcacttttttgtctcccctttggg

Docket/App No.: 3258.1008-001

Title: HMGB1 Combination Therapies

Inventors: Walter Newman

1	mgkgdpkkpr gkmssyaffv q	tcreehkkk hpdasvnfse fskkcserwk tmsakekgkf	rat # P07155
1	mgkgdpkkpr gkmssyaffv q	tcreehkkk hpdasvnfse fskkcserwk tmsakekgkf	mouse #AAA20508
1	mgkgdpkkpt gkmssyaffv g	tcreehkkk hpdasvnfse fskkcserwk tmsakekgkf	human #AAA64970
	A box		

61 edmakadkar yeremktyip pkgetkkkfk dpnapkrpps affifcseyr pkikgehpgl rat
61 edmakadkar yeremktyip pkgetkkkfk dpnapkrpps affifcseyr pkikgehpgl mouse
61 edmakadkar yeremktyip pkgetkkkfk dpnapkrlps affifcseyr pkikgehpgl human

B box

121 sigdvakkig emwnntaadd kqpyekkaak lkekyekdia ayrakgkpda akkgvvkaek rat
121 sigdvakkig emwnntaadd kqpyekkaak lkekyekdia ayrakgkpda akkgvvkaek mouse
121 sigdvakkig emwnntaadd kqpyekkaak lkekyekdia ayrakgkpda akkgvvkaek human

181 skkkkeeedd eedeedeese eeeede deee dddde *rat*181 skkkkeeedd eedeedeese eeeede deee dddde *mouse*181 skkkkeeedd eedeedeese edeedeedee dddde *human* 

FIG. 13

Inventors: Walter Newman

### FIG. 14A

# NG 000897 DNA (bases 150-797)

# FIG. 14B

# NG 000897 Protein

MGKGDPKKPT GKMSSYAFFV QTCREEHKKK HPDASVNFSE FSKKCSERWK TMSAKEKGKF EDMAKADKAR YEREMKTYIP PKGETKKKFK DPNAPKRLPS AFFLFCSEYR PKIKGEHPGL SIGDVAKKLG EMWNNTAADD KQPYEKKAAK LKEKYEKDIA AYRAKGKPDA AKKGVVKAEK SKKKKEEEED EEDEEDEEEE EDEEDEEDEE

# FIG. 14C

# **AF076674 DNA** (bases 1-633)

ATGGGCAAAG GAGATCCTAA GAAGCCGAGA GGCAAAATGT CATCATATGC ATTTTTTGTG CAAACTTGTC GGGAGGAGCA TAAGAAGAAG CACTCAGATG CTTCAGTCAA CTTCTCAGAG TTTTCTAACA AGTGCTCAGA GAGGTGGAAG ACCATGTCTG CTAAAGAGAA AGGAAAATTT GAGGATATGG CAAAGGCGAA CAAGACCCAT TATGAAAGAC AAATGAAAAC CTATATCCCT CCCAAAGGGG AGACAAAAAA GAAGTTCAAG GATCCCAATG CACCCAAGAG GCCTCCTTCG GCCTTCTCC TGTTCTGCTC TGAGTATCAC CCAAAAATCA AAGGAGAACA TCCTGGCCTG TCCATTGGTG ATGTTGCGAA GAAACTGGGA GAGATGTGGA ATAACACTGC TGCAGATGAC AAGCAGCCTG GTGAAAAGAA GGCTGCGAAG CTGAAGGAAA AATACGAAAA GGATATTGCT GCATATCAAG CTAAAGGAAA GCCTGAGGCA GCAAAAAAA GGAGATGTCAA AGCAGCATGA AGCAGGAAAA AGCAAGAAAA AGCAAGAAAA AGCAAGAAGA GGAGGAAGAT GAGGAAGATG AAGAGGATGA GGAGGAAGAA GATGAAGAAG ATGAAGAAGA TGATGATGAT GAA

# FIG. 14D

### AF076674 Protein

MGKGDPKKPR GKMSSYAFFV QTCREEHKKK HSDASVNFSE FSNKCSERWK TMSAKEKGKF EDMAKADKTH YERQMKTYIP PKGETKKKFK DPNAPKRPPS AFFLFCSEYH PKIKGEHPGL SIGDVAKKLG EMWNNTAADD KQPGEKKAAK LKEKYEKDIA AYQAKGKPEA AKKGVVKAEK SKKKKEEEED EEDEEDEEE DEEDEEDDDD E

Inventors: Walter Newman

### FIG. 14E

# **AF076676 DNA** (bases 1-564)

ATGGGCAAAG GAGACCCTAA GAAGCCGAGA GGCAAAATGT CATCATATGC ATTTTTTGTG CAAACTTGTC GGGAGGAGTG TAAGAAGAAG CACCCAGATG CTTCAGTCAA CTTCTCAGAG TTTTCTAAGA AGTGCTCAGA GAGGTGGAAG GCCATGTCTG CTAAAGATAA AGGAAAATTT GAAGATATGG CAAAGGTGGA CAAAGACCGT TATGAAAGAG AAATGAAAAC CTATATCCCT CCTAAAGGGG AGACAAAAAA GAAGTTCGAG GATTCCAATG CACCCAAGAG GCCTCCTTCG GCCTTTTGC TGTTCTGCTC TGAGTATTGC CCAAAAATCA AAGGAGAGCA TCCTGGCCTG CCTATTAGCG ATGTTGCAAA GAAACTGGTA GAGATGTGGA ATAACACTTT TGCAGATGAC AAGCAGCTTT GTGAAAAAAA GGCTGCAAAG GCCTGCAAAG GCCTGAAGGAAA AATACAAAAA GGATACAGCT ACATATCGAG CTAAAGGAAA AGCAAGAAAAA AGCAAGAAAAA AGCAAGAAAAA AGCAAGAAAAA AGCAAGAAAAA AGCAAGAAAAA AGCAAGGAAAA AGCAAGAAAAA AGCAAGGAAAA AGCAAGGAAAA AGCAAGAAAAA AGCAAGGAAGA GGAG

#### FIG. 14F

#### AF076676 Protein

MGKGDPKKPR GKMSSYAFFV QTCREECKKK HPDASVNFSE FSKKCSERWK AMSAKDKGKF EDMAKVDKDR YEREMKTYIP PKGETKKKFE DSNAPKRPPS AFLLFCSEYC PKIKGEHPGL PISDVAKKLV EMWNNTFADD KQLCEKKAAK LKEKYKKDTA TYRAKGKPDA AKKGVVKAEK SKKKKEEE

# FIG. 14G

# AC010149 DNA (bases 75503-76117)

ATGGACAAAG CAGATCCTAA GAAGCTGAGA GGTGAAATGT TATCATATGC ATTTTTTGTG CAAACTTGTC AGGAGGAGCA TAAGAAGAAG AACCCAGATG CTTCAGTCAA GTTCTCAGAG TTTTTAAAGA AGTGCTCAGA GACATGGAAG ACCATTTTTG CTAAAGAGAA AGGAAAATTT GAAGATATGG CAAAGGCGGA CAAGGCCCAT TATGAAAGAG AAATGAAAAC CTATATCCCT CCTAAAGGGG AGAAAAAAAA GAAGTTCAAG GATCCCAATG CACCCAAGAG GCCTCCTTTG GCCTTTTCC TGTTCTGCTC TGAGTATCGC CCAAAAATCA AAGGAGAACA TCCTGGCCTG TCCATTGATG ATGTTGTGAA GAAACTGGCA GGGATGTGGA ATAACACCGC TGCAGCTGAC AAGCAGTTTT ATGAAAAGAA GGCTGCAAAG CTGAAGGAAA AATACAAAAA GGATATTGCT GCATATCGAG CTAAAGGAAA GCCTAATTCA GCAAAAAAAA GAGTTGTCAA GGCTGAAAAA AGCAAGAAAA AGAAGGAAGA GGAAGAAGAT GAAGAGGATG AACAAGAGA GGAAAATGAA GAAGATGAT ATAAA

### FIG. 14H

### AC010149 Protein

MDKADPKKLR GEMLSYAFFV QTCQEEHKKK NPDASVKFSE FLKKCSETWK TIFAKEKGKF EDMAKADKAH YEREMKTYIP PKGEKKKKFK DPNAPKRPPL AFFLFCSEYR PKIKGEHPGL SIDDVVKKLA GMWNNTAAAD KQFYEKKAAK LKEKYKKDIA AYRAKGKPNS AKKRVVKAEK SKKKKEEEED EEDEQEEENE EDDDK Docket/App No.: 3258.1008-001

Title: HMGB1 Combination Therapies

Inventors: Walter Newman

#### FIG. 14I

### **AF165168 DNA** (bases 729-968)

ATGGGCAAAG GAGATCCTAA GAAGCCGAGA GGCAAAATGT CATCATGTGC ATTTTTTGTG CAAACTTGTT GGGAGGAGCA TAAGAAGCAG TACCCAGATG CTTCAATCAA CTTCTCAGAG TTTTCTCAGA AGTGCCCAGA GACGTGGAAG ACCACGATTG CTAAAGAGAA AGGAAAATTT GAAGATATGC CAAAGGCAGA CAAGGCCCAT TATGAAAGAG AAATGAAAAC CTATATACCC

#### FIG. 14J

# AF165168 Protein

MGKGDPKKPR GKMSSCAFFV QTCWEEHKKQ YPDASINFSE FSQKCPETWK TTIAKEKGKF EDMPKADKAH YEREMKTYIP

#### FIG. 14K

# **XM 063129 DNA** (bases 319-558)

AAACAGAGAG GCAAAATGCC ATCGTATGTA TTTTGTGTGC AAACTTGTCC GGAGGAGCGT AAGAAGAAAC ACCCAGATGC TTCAGTCAAC TTCTCAGAGT TTTCTAAGAA GTGCTTAGTG AGGGGGAAGA CCATGTCTGC TAAAGAGAAA GGACAATTTG AAGCTATGGC AAGGGCAGAC AAGGCCCGTT ACGAAAGAGA AATGAAAACA TATATCCCTC CTAAAGGGGA GACAAAAAAA

### FIG. 14L

# XM 063129 Protein

KQRGKMPSYV FCVQTCPEER KKKHPDASVN FSEFSKKCLV RGKTMSAKEK GQFEAMARAD KARYEREMKT YIPPKGETKK

#### FIG. 14M

# XM 066789 DNA (bases 1-258)

ATGGGCAAAA GAGACCCTAA GCAGCCAAGA GGCAAAATGT CATCATATGC ATTTTTTGTG CAAACTGCTC AGGAGGAGCA CAAGAAGAAA CAACTAGATG CTTCAGTCAG TTTCTCAGAG TTTTCTAAGA ACTGCTCAGA GAGGTGGAAG ACCATGTCTG TTAAAGAGAA AGGAAAAATTT GAAGACATGG CAAAGGCAGA CAAGGCCTGT TATGAAAGAG AAATGAAAAT ATATCCCTAC TTAAAGGGGA GACAAAAA

### FIG. 14N

# XM 066789 Protein

MGKRDPKQPR GKMSSYAFFV QTĄQEEHKKK QLDASVSFSE FSKNCSERWK TMSVKEKGKF EDMAKADKAC YEREMKIYPY LKGRQK

Inventors: Walter Newman

# FIG. 140

# **AF165167 DNA** (bases 456-666)

ATGGGCAAAG GAGACCCTAA GAAGCCAAGA GAGAAAATGC CATCATATGC ATTTTTTGTG CAAACTTGTA GGGAGGCACA TAAGAACAAA CATCCAGATG CTTCAGTCAA CTCCTCAGAG TTTTCTAAGA AGTGCTCAGA GAGGTGGAAG ACCATGCCTA CTAAACAGAA AGGAAAATTC GAAGATATGG CAAAGGCAGA CAGGGCCCAT A

# FIG. 14P

# AF165167 Protein

MGKGDPKKPR EKMPSYAFFV QTCREAHKNK HPDASVNSSE FSKKCSERWK TMPTKQKGKF EDMAKADRAH